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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,519	11/28/2001	Vassiliki A. Boussiotis	RPI-011CPCN	3634

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LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,519	BOUSSIOTIS ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *92-100,102 and 103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *92-100, 102, 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HC

DETAILED ACTION

1. Applicant's amendments, filed 12/21/04, have been entered.
Claims 92-100 have been amended.
Claims 101 and 104-107 have been canceled. Claims 1-91 have been canceled previously.

Claims 92-100 and 102-103 are pending and being acted upon presently.

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Applicant's amended claims have obviated the previous rejections under 35 U.S.C. 112, first paragraph, written description and enablement.

4. Applicant's amended claims, filed have obviated the previous provisional rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,451,305.

5. Upon amending the claims to recite "CD59", the following rejection is set forth.

Claims 92-100 and 102-103 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the instant disclosure in the absence of either in vitro and in vivo experimental accurately reflects the relative efficacy of the claimed therapeutic strategy "to stimulate T cell responses to a tumor cell modified with CD59 and an CD28 or CTLA4 ligand".

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

It has been art-recognized experience that immunotherapy for cancer has been limited. Results obtained under controlled conditions and in inbred animals often differ from the clinical response obtained in patients. This applies in particular to strategies based on immune responses, including strategies drawn to cancer therapy. It is difficult to predict whether therapeutic success will be achieved, even if a significant increase in anti-tumor CTL obtained by immunization. Tumor burden and antigenic drift continue to present serious burdens for successful cancer therapy in vivo. Tumors are classified as immunogenic or non-immunogenic, solid or hematological in nature. Effective cancer strategies should be design to deal effectively with the nature of each of these classifications. For experimental anti-tumor immunization in animals, one usually immunizes a normal animal and the effect is evaluated by the resistance to a tumor cell. For human patients, one would have to stimulate immune defense or organisms that have often carried a large tumor cell challenge.

With respect to immunotherapy of cancer with genetically modified tumor vaccines, Gilboa (Seminars in Oncology 23: 101-107, 1996) note that whereas animal studies have attempted to approximate as closely as possible the condition prevailing in the cancer patient, animal studies cannot accurately reproduce the complexity and variability exhibited among human patients (see entire document, including page 104, column 2, paragraph 2). Gilboa further discusses the limitations Toward Clinical Assessment OF GMTV In Cancer Patients (see pages 104-105).

With respect to the role of CD59 on the cell surface of tumor cells, the following is noted.

Yu et al. (Clin. Exp. Immunol 115 : 13 – 18, 1999) describe that transfecting tumor cells with CD59 was effective in protecting tumor cells from cell lysis via complement (See entire document, including Summary, Results and Discussion).
In addition, Yu et al. further suggest that the skilled artisan should consider neutralizing CD59 or modulating CD59 on tumor in therapeutic regimens of treating tumors (see Discussion on pages 16-17).

In a similar fashion, Brasoveanu et al. (Int. J. Cancer 61: 548 –556. 1995) disclose that their data demonstrate that CD59 expressed on human melanoma cells might regulate host-tumor interaction by protecting neoplastic cells from complement-mediated lysis (see entire document, including Abstract and Discussion).

In addition, Brasoveanu et al. indicate that observations reinforce experimental evidence suggesting that CD59 should not be considered a potential ligand for CD2 (see page 555, columns 1-2, overlapping paragraph).

Brasoveanu et al. concludes that CD59 expressed by melanoma cells does not play a functional role in cellmediated cytotoxicity of neoplastice cells of the melanocytic lineage; however CD59 might be involved in melanoma-host interaction by preventing the complement-mediated lysis of melanoma cells.

The specification does not adequately teach how to effectively use CD59-modified tumor cells to stimulate effective T cell responses to tumor cells in humans. The specification does not teach how to extrapolate data obtained from certain modified tumor cells with other molecules (e.g. LFA-3 and B7) to the development of effective in vivo human therapeutic methods with CD59-modified tumor cells, encompassed by the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the CD59-modified tumor cells to stimulate appropriate T cell responses to tumor cells.

There is insufficient objective evidence that CD59-modified tumor cells would be expected to stimulate appropriate anti-tumor responses, given that CD59 appears to protect tumor cells from host immune responses and that CD59 should not be considered a potential ligand for CD2, as evidenced by Yu et al. (Clin. Exp. Immunol 115: 13-18, 1999) and Brasoveanu et al. (Int. J. Cancer 61: 548 –556. 1995).

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective genetically modified tumor cells to induce effective T cell responses to tumor cells, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for stimulating effective T cells responses to CD59-modified tumor cells.

6. No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
April 11, 2005